REMARKS

With the entry of the present amendments, claims 1, 3-21, 33, 55-62, 73-75, 82, 85 and 87-99 are pending in the application. Claims 2, 22-32, 34-54, 63-72, 76-81, 83, 84 and 86 have been cancelled. Claims 55, 56, 73-75, 82, 85, and 87-90 have been amended. New claims 91-99 have been added. Support for the claim amendments and new claims may be found throughout the specification as filed including, but not limited to, paragraphs 0143, 0145, 0163 and 0170-0172; pages 44-45 (Example 15); and figures 7-9. Claims 1, 3-21, and 33 have been allowed.

As discussed below, the present amendment now places all of the pending claims in the application in condition for allowance.

CLAIM REJECTIONS

In the Final Office Action, claims 55-62, 73-82, 86, and 87 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Applicants respectfully traverse this rejection.

In the final Office Action, the Examiner stated that the specification does not support the conservative variant binding to acute myeloid leukemia cells, as recited in claim 55,

> because the limitation would also include peptides which bind selectively to acute myeloid leukemia cells to the exclusion of chronic myeloid leukemia cells, or the exclusion of normal myeloid cells, and the specification does not provide a single peptide which would bind in a specific manner to acute myeloid cells to the exclusion of either chronic myeloid leukemia cells or normal myeloid cells.

The rejection was reiterated in the Advisory Action. However, in the Advisory Action, the Examiner acknowledges that the specification does provide adequate support for the limitation that SEQ ID NO 1 induces differentiation of acute myeloid leukemia cells, as shown by the evidence provided in Table 7.

Although Applicants respectfully disagree with the Examiner's rejection, Applicants have amended claim 55 to recite polypeptides comprising a sequence selected from one of SEQ ID NOS 1, 2, 3, 16 and 22 having one or more conservative amino acid substitutions, "wherein the

polypeptide induces differentiation of acute myeloid leukemia cells into mature blood cells," in order to expedite the prosecution of this application. Applicants note that the data presented in Figures 7-9 support this limitation for SEQ ID NOS. 1 (G5 12-8B), 2 (B6 12-8B), 3 (A2 no cyst) and 16 (B4(1) – as identified in paragraph 0145). Support for the amendment with regard to SEQ ID NO 22 is provided in paragraph 0143.

Applicants further note that one of ordinary skill in the art would recognize that the Applicants were in possession of the polypeptide variants having one or more conservative amino acid substitutions recited in the amended claims because the genus of polypeptides recited in amended claim 55 is strictly circumscribed with respect to both structure and function. The permitted variance between the claimed genus of polypeptides and a given literal polypeptide is strictly circumscribed because the genus includes only those polypeptides that differ from the literal polypeptide sequence by conservative amino acid substitutions. The application clearly defines a conservative amino acid substitution as a substitution where one amino acid residue is replaced by another, *biologically similar* residue. (See, paragraph 0051, emphasis added.) In fact, the concept of conservative amino acid substitutions is well known. For example, the Biology-Online Dictionary defines "Conservative Substitution" as follows: "In a gene product, a substitution of one amino acid with another with generally similar properties (size, hydrophobicity, etc), such that the overall functioning is likely not to be seriously affected." Thus, the vary nature of a *conservative* amino acid substitution strictly limits the possible structural variation. Regarding claims 56-62, Applicants further note that the degree of allowed structural variation in the polypeptides of the claimed genus is even more strictly limited, either by the recitation of specific properties which the substituted amino acid residues must possess (e.g., hydrophobicity or polarity) or by the specification of particular amino acid residues which may be involved in a conservative substitution. In addition, the two functional limitations in amended claim 55 that the polypeptides must bind to acute myeloid leukemia cells *and* induce differentiation of acute myeloid leukemia cells, further ensure that the claimed variants of the polypeptides are sufficiently limited in view of the disclosure in the pending application.

Finally, it is clear that Applicants were in possession of the polypeptides of the structurally and functionally-circumscribed genus recited in the amended claims at the time the

invention was made. Applicants have not only identified the literal sequences for many member of the genus, but have also clearly explained the means by which conservative amino acid substitutions are identified. Specifically, paragraph [0052] of the application provides a specific example of a software program (LASERGENE) that was available at the time the invention was made that would enable Applicants to identify conservative amino acid substitutions for the literal polypeptides, and thereby identify the members of the genus. In addition, Applicants have provided a description of experiments that may be conducted to identify those structural variants that possess the recited functional limitations (e.g., binding to acute myeloid leukemia cells and inducing differentiation of acute myeloid leukemia cells). (See, for example, Example 15.) It follows that Applicants clearly had possession of the claimed subject matter, including the recited sequence variants, at the time this invention was made.

For these reasons, Applicants respectfully submit that claim 55 and all of the claims depending therefrom are now in condition for allowance and respectfully request that the rejections to these claims be withdrawn.

CLAIM OBJECTIONS

In the Final Office Action, the Examiner objected to claim 88 due to an apparent typographical error. In the response to the Advisory Action filed on July 5, 2006, Applicants corrected the typographical error in claim 88. No other objections or rejections were raised against claim 88. Applicants have now amended claim 88 to recite sequences having one or more conservative amino acid substitutions.

As a preliminary matter, Applicants note that the claim includes the limitation that the peptides specifically bind to normal bone marrow cells (which would include normal myeloid cells) but not to acute myeloid leukemia cells, as supported by the disclosure in paragraph 0154 of the specification. Therefore, the claims do not suffer from any alleged deficiency regarding a lack of disclosure of peptides that exhibit specific binding to normal myeloid cells to the exclusion of acute myeloid cells. Applicants further note that it is clear that the inventors were in possession of the polypeptide variants having one or more conservative amino acid substitutions recited in claim 88 because the genus of polypeptides recited this claim is strictly circumscribed

with respect to both structure and function, as described above with respect to claim 55. Therefore, Applicants submit that claim 88 and all the claims depending therefrom are now in condition for allowance and respectfully request that the objection be withdrawn.

NEW CLAIMS

With the entry of the present amendments, new claims 91-99 have been added to the pending application. Applicants respectfully submit that these new claims are in condition for allowance for the following reasons.

New claims 92 and 98 depend from claim 55. Thus, these claims are in condition for allowance for the reasons presented above with respect to claim 55, from which they depend.

New claim 91 depends from claim 88. Thus, claim 91 is in condition for allowance for the reasons presented above with respect to claim 88, from which it depends.

New claim 93 recites isolated polypeptides comprising amino acid sequences selected from SEQ ID NOS 13, 15, and 21 having one or more conservative amino acid substitutions, wherein the polypeptides bind to acute myeloid leukemia cells and further wherein the polypeptides induce differentiation of bone marrow cells obtained from a patient with acute myeloid leukemia. Support for this claim may be found in Example 15 of the application. It is clear that Applicants were in possession of the polypeptide variants having one or more conservative amino acid substitutions recited in claim 98 because the genus of polypeptides recited this claim is strictly circumscribed with respect to both structure and function, as described above with respect to claim 55.

New claim 99 recites isolated polypeptides comprising amino acid sequences selected from SEQ ID NO 16 having one or more conservative amino acid substitutions, wherein the polypeptides bind to acute myeloid leukemia cells but not to normal bone marrow cells. Support for this claim may be found in paragraph 0145 of the specification. It is clear that Applicants were in possession of the polypeptide variants having one or more conservative amino acid substitutions recited in claim 99 because the genus of polypeptides recited this claim is strictly

circumscribed with respect to both structure and function, as described above with respect to claim 55.

For the foregoing reasons Applicants respectfully submit that all of the claims pending in the application are now in condition for allowance. Consequently, Applicants respectfully request that Examiner withdraw all of the rejections and allow the application to issue. The Examiner is invited to contact the undersigned by telephone if it is thought that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

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